Translation

PCT/EP2003/012531

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference U30035PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP2003/012531	International filing date (*day/month/year*) 10 November 2003 (10.11.2003)	Priority date (*day/month/year*) 16 November 2002 (16.11.2002)
International Patent Classification (IPC) or national classification and IPC G01N 33/68		
Applicant DADE BEHRING MARBURG GMBH		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 16 June 2004 (16.06.2004)	Date of completion of this report 17 March 2005 (17.03.2005)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

Form PCT/IPEA/409 (cover sheet) (July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP2003/012531

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed

☒ the description:
pages 1-61, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the claims:
pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages 7 (part), 8-27 / 1-6, 7 (part), filed with the letter of 18.08.2004 / 08.10.2004

☒ the drawings:
pages 1/18-18/18, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 19-21

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 19-21 are so unclear that no meaningful opinion could be formed *(specify)*:

See supplemental sheet

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Box III.1

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. PCT Article 6

The application fails to meet the requirements of PCT Article 6 because claims 19 to 21 are not clear.

1.1 Claims 19 to 21 cover a diagnostic kit that contains "means". The qualification "(means) for carrying out the method according to one of claims 1 to 18" does not have any limiting significance for the kit according to claims 19 to 21. The "means" are therefore the only technical feature of the diagnostic kit, and the term covers such an infinite number of possibilities (for example, an Eppendorf tip, a buffer, a plate, etc.) that the claims seem unclear and too broad (PCT Article 6). The lack of clarity is such that it is not possible to carry out a meaningful search covering the full range of subject matter for which protection is sought.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-18, 22-27	YES
	Claims		NO
Inventive step (IS)	Claims	1-18, 22-27	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-18, 22-27	YES
	Claims		NO

2. Citations and explanations

1. Prior art

Reference is made to the following documents:

D1: WO-A-0156593

D2: D. Maglione et al., *Il Farmaco*, **2000**, Vol. 55, pages 165-167

D3: A. Luttun et al., *Nature Medicine*, **2002**, Vol. 8, No. 8, pages 831-840

Document **D1** discloses the use of placenta growth factor (PlGF) for the treatment of acute cardiovascular diseases (claims 1 to 25 and examples 1 to 4).

Document **D2** describes the angiogenic activity of PlGF. Preliminary studies also show that PlGF has a protective effect against myocardial lesions (see the abstract, figure 1, and tables 1 and 2).

Document **D3** shows that PlGF promotes angiogenesis and arteriogenesis (see the abstract, figures 1 and 2, and table 1).

2. PCT Article 33(2) and 33(3)

2.1 Document **D1**, which is considered to be the prior art closest

to the subject matter of claim 1, discloses the use of placenta growth factor (PlGF) for the treatment of acute cardiovascular diseases (claims 1 to 25 and examples 1 to 4).

The subject matter of claim 1 of the present application differs from that of **D1** in that placenta growth factor is used as a marker for diagnosing acute cardiovascular diseases.

The subject matter of claim 1 is therefore novel (PCT Article 33(2)).

2.2 The problem addressed by the present invention can thus be seen as that of providing a method for diagnosing acute cardiovascular diseases.

The solution proposed in claim 1 of the present application involves an inventive step (PCT Article 33(3)) because none of the cited documents describe the use of PlGF as a diagnostic target protein. The invention according to claim 1 is therefore a novel application for PlGF. Taking D1 as a starting point and adducing either D2 or D3 in conjunction with the common general knowledge in the art, a skilled person would find nothing to suggest the claimed solution. Claim 1 therefore involves an inventive step.

2.3 Claims 2 to 18 and 22 to 27 are dependent on claim 1 and therefore also meet the PCT requirements in respect of novelty and inventive step (PCT Article 33(2) and 33(3)).

3. PCT Article 33(4)

An *in vitro* method for diagnosing acute cardiovascular diseases comprising a step for determining the concentration of the PlGF marker in a sample, as defined in claims 1 to 18 and 22 to 27, is industrially applicable because the subject matter can be made or used in the biomedical industry.